Two miRNA Clusters Reveal Alternative Paths in Late-Stage Reprogramming.

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Public Summary:

Scientific Abstract:
Ectopic expression of specific factors such as Oct4, Sox2, and Klf4 (OSK) is sufficient to reprogram somatic cells into induced pluripotent stem cells (iPSCs). In this study, we examine the paths taken by cells during the reprogramming process by following the transcriptional activation of two pluripotent miRNA clusters (mir-290 and mir-302) in individual cells in vivo and in vitro with knockin reporters. During embryonic development and embryonic stem cell differentiation, all cells sequentially expressed mir-290 and mir-302. In contrast, during OSK-induced reprogramming, cells activated the miRNA loci in a stochastic, nonordered manner. However, the addition of Sall4 to the OSK cocktail led to a consistent reverse sequence of locus activation (mir-302 then mir-290) and increased reprogramming efficiency. These results demonstrate that cells can follow multiple paths during the late stages of reprogramming, and that the trajectory of any individual cell is strongly influenced by the combination of factors introduced.